

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Friedman et al.

Appl. No.: 08/485,943

Filed: June 7, 1995

For: Modulators of Body Weight,
Corresponding Nucleic Acids and
Proteins, and Diagnostic and
Therapeutic Uses Thereof

Confirmation No.: 6144

Art Unit: 1632

Examiner: Wilson, Michael C.

Atty. Docket: 1315US-CIP05

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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Applicants request review of the rejections in the above-identified application. No amendments are being filed with this request. An Amendment and Response to the Office Action mailed January 22, 2008 was filed on June 19, 2008. Applicants are not aware of any reason why the June 19, 2008 amendment will not be entered, therefore, this Request refers to the amended claims.

This request is being filed with a notice of appeal. The review is requested for the following remarks.

Claims 124, 132-137, 139-143, 145-150, 155-159, and 163-174 are pending.

Rejection Under 35 U.S.C. § 112, 1st paragraph, Enablement

Claims 124, 132-137, 139-143, 145-150, 155-159, and 163-174 stand rejected under 35 U.S.C. § 112, 1st paragraph as lacking enablement. Specifically, the Examiner continues to predicate his rejection on the allegation that “overall, the specification does not overcome the unpredictability in the art by teaching the specific combination of vector, promoter, dosage, and route of administration required to target ob expression to fat cell or how to express ob protein so it will target the tissue that mediates a reduction in body weight (see Office Action mailed January 22, 2008 (“Office Action”), Page 10, second complete paragraph).

Targeting the claimed vectors to a particular tissue or cell type is not a limitation found in the instant claims, and is not a requirement for practicing the claimed methods (see, e.g., Applicant’s Response filed October 31, 2007, page 19, line,. Indeed, as explained previously by Applicant, the issue is irrelevant insofar as “non-targeting” of the recited OB protein, which constitutes a secreted and circulating factor as taught in the instant specification, to tissue that expresses endogenous OB protein, would not negate a therapeutic effect as a matter of course (see, e.g., Applicant’s response filed October 31, 2007, page 19, line 6, through page 20, line 7). In fact, the Examiner has never provided any evidence to the contrary. Thus, the examiner’s

assertion not only lacks factual and scientific merit or evidentiary support, but also constitutes “a broad allegation that the application disclosure is speculative, coupled with a recitation of various difficulties which might be encountered in attempting to put it into practice, and a further assertion that there might be still other difficulties which could not be foreseen,” which the Courts have held is not considered to constitute “a sufficiently definite statement of a basis for rejection.” *In re Chilowsky*, 229 F.2d 457,462 (C.C.P.A. 1956).

With respect to the references cited by the Examiner that allegedly related to the,general unpredictability in the art (see Office Action, page 5, line 16, through page 7, line 18), as Applicant has explained previously, such allegations have no relevance to the specific facts of the instant case; the references are completely silent with regard the question of with respect to the nucleic acids, vectors, OB proteins expressed thereby, and therapeutic effect as recited in the instant claims (see, e.g., Applicant’s response filed October 31, 2007, page 19, line 6, through page 20, line 7). As explained in Applicant’s previous response(s) the Examiner’s continued reliance on such generalizations are unavailing and at odds with principles well-established by the Courts, which set forth that the question of enablement, particularly the issue of undue experimentation, must be decided on the facts of the case (see, e.g., *Ex Parte Goeddel*, 5 U.S.P.Q.2d 1449, 1450 (Bd. Pt. App. & Int. 1985), and *Ex Parte Kung*, 17 U.S.P.Q.2d 1545, 1546 (Bd. Pt. App. & Int. 1989)(see, e.g., Applicant’s response dated October 31, 2007, page 21, lines 1 -16). Thus, the Examiner’s assertions are factually and legally errant.

With respect to post-filing references cited by the Examiner, Applicant has repeatedly pointed out that such references support, rather than negate, Applicant’s rebuttal of the rejection. The references demonstrate that each particular combination of vector dosage, promoter usage, and administration route, resulted in effects as instantly claimed, and therefore obviate the Examiner’s allegation concerning unpredictability of selecting a suitable combination of such elements from among those disclosed in Applicant’s specification and those available in the art for practicing the instant claims (see, e.g., Applicant’s response filed October 31, 2007, page 20, lines 8 – 30).

With respect to the Examiner’s allegation that Applicant has attempted to “establish the state of the art” by virtue of Applicant’s rebuttal of the Examiner’s comments, described above, Applicant notes that such comments are not attempts at such characterization, but constitute a response to the Examiner’s characterization and application of the alleged disclosure of in the references as they are alleged to relate to the instant claims. Applicant’s further note that Applicant’s comments were not provided prior to the Examiner’s characterization and application of that characterization in his maintained enablement rejection. Furthermore, even assuming *arguendo* that Applicant’s rebuttal of the Examiner’s characterization and application of these post-filing references to the enablement rejection may be properly construed as an attempt to “establish the state of the art”, Applicant notes that it is well settled that post-filing references may, in fact, be relied upon to demonstrate the extent of an enabling disclosure. See *Amgen Inc. v. Hoechst Marion Roussel, Inc*, 314 F.3d 1313 (Fed. Cir. 2003); *Gould v. Quigg*, 822 F.2d 1074, 1078 (Fed. Cir. 1987). Furthermore, post-filing date information may be used to prove the accuracy of statements already in the specification, i.e., to show that the disclosure was in fact enabling when filed. See *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995). Thus the examiner’s assertion is factually and legally errant.

With respect to the Examiner’s allegation that “the specification does not provide an enabled use for decreasing the body weight of a wild-type mammal (having normal weight)”, Applicant refers to Example 8: page 125, line 25, through page 126, line 3 (including Table 1);

and Figure 28A through 28F, which demonstrate that wild type OB polypeptides of Applicants application as originally filed, which demonstrate that “[i]n wild-type mice there was a small but significant decrease in body weight following administration of the recombinant ob protein.” Thus, the Examiner’s assertion is factually and scientifically errant.

Additionally, the Examiner continues to assert that the instant claims “encompass using analogs that agonize or antagonize the function of the ob protein to decrease body weight, which is not enabled,” and that the instant claims “do not clearly set forth that the mammal exhibits a decrease in body weight or that the therapeutic effect is decrease in body weight. (see Office Action, page 18, line 18 through page 19, line 5). Applicant has repeatedly noted that the instant claims are directed to methods of decreasing (and not increasing) body weight in mammals administered the recited OB-encoding vectors, which vectors encode OB proteins that are capable of decreasing body (see, e.g., Applicant’s response filed October 31, 2007, page 22, lines 17 – 27); thus, ob antagonists are not encompassed by the claims. Accordingly, the Examiner’s assertion is factually and legally errant.

The Examiner also continues to assert in his enablement rejection that a definition of “conservative” and “nonconservative” substitutions is required (see Office Action, page 19, lines 6-15). Applicant has repeatedly noted that there is no recitation in the claims specifying a “conservative or a non-conservative substitution”, and thus no definition is required concerning these terms in order to enable the claims; even assuming *arguendo* that they would be required, such terms were well-known and recognized in the art at the time of the effective filing date of the instant application (see, e.g., Applicant’s response filed October 31, 2007, page 22, line 29, through page 23, line 8). In the instant Office Action, the Examiner now responds by stating that because Salvator (2001) allegedly teaches that “the body weight control functions [are] confined to amino acids 106-140”, which is allegedly not taught in Applicant’s disclosure. This alleged teaching concerning a minimal active OB fragment has absolutely no relevance to the question concerning a requirement for a definition of the terms “conservative substitution” and “nonconservative substitution” and does not serve as an availing rebuttal to Applicant’s arguments. Accordingly, the Examiner’s assertion is factually and legally errant.

Rejection Under 35 U.S.C. § 112, 1st paragraph, New Matter

Claims 124, 132-137, 139-143, 145-150, 155-159, and 163-174 stand rejected under 35 U.S.C. § 112, 1st paragraph as allegedly containing new matter.

All of the new matter rejections found in the instant Office Action have been repeatedly addressed in Applicants previous arguments (see, e.g., Applicant’s response filed October 31, 2007: page 24, lines 1-22 concerning the phrase “operatively linked to a promoter”; page 25, line 1, page 29, line 30, concerning all substitutions, etc., currently recited in the claims and maintained as rejected as new matter). Specifically, Applicant has noted that a representative number of species encompassed by the claims is disclosed in the application as originally filed. With respect to specific positions recited as available for substitution, all such positions are disclosed in the specification in the portions of the specification previously pointed to by Applicant. When taken collectively, all of the drawings, excerpts from written text of the specification, and the sequences in the Sequence Listing that Applicant has previously pointed to disclose and support every position and SEQ ID NO. recited in the instant claims.

In this regard, Applicant notes that it is well settled that “[h]ow the specification meets the requirements of section 112 is not material.” *In re Herschler*, 591 F.2d693 (CCPA, 1979). Furthermore, MPEP 2163.02 states that “The subject matter of the claim need not be described

literally (i.e., using the same terms or in haec verba) in order for the disclosure to satisfy the description requirement.” Rather, it is sufficient if the “description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.” *Id.* MPEP 2163.02 further states that

[u]nder *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon “reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter.” *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)).

Thus, even assuming *arguendo* that *in haec verba* support for the claim limitations at issue is not present in the specification, such support is not required; rather, written description support need be only so clear such that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented processes including those limitations. Further, “an Applicant satisfies the written description requirement by describing all of the features of a claim in a manner that “reasonably conveys” to one of ordinary skill in the art that the Applicant possessed the claimed invention as a whole. (MPEP § 2163(I)). To do so, an Applicant may rely on words, structures, figures, diagrams, and formulae of the disclosure. (MPEP §§ 2163(I), 2163.02). A patent specification satisfies the written description requirement when it discloses a claimed invention in sufficient detail so that one skilled in the art can “reasonably conclude” that the inventor had possession of the claimed invention.”

Accordingly, the Examiner’s new matter rejection is factually and legally errant.

Rejection Under 35 U.S.C. § 112, 1st paragraph, Written Description

Claims 124, 132-137, 139-143, 145-150, 155-159, and 163-174 stand rejected under 35 U.S.C. § 112, 1st paragraph as allegedly failing to comply with the written description requirement. Applicant has previously responded to this rejection in full (see, e.g., Applicant’s response filed October 31, 2007, page 30, line 1, through page 31, line 2). Applicant submits that the Examiner’s repeated rejection is factually and legally errant for the reasons provided in Applicant previous response, at least.

As discussed in Applicants’ previous response, the specification does not expressly or implicitly disclose that targeting of fat cells is the only administration modality by which the instantly claimed methods may be practiced; the cited portion states the “the ob gene could be introduced into human fat cells to develop gene therapy for obesity.” This statement does not negate any other targeting modality, including, to specific targeting of any tissue or cell type at all, as described above, in order to practice the claimed methods. Furthermore, it is well established that an Applicant’s claims to a disclosed invention is not bound by any suggested theory or mechanism for the inventions operation, even if such suggested theory is ultimately found to be incorrect.

Furthermore, contrary to the Examiner’s continued assertion, the instant specification provides ample description of determination of a therapeutically effective amount, of example at

page 72, lines 5-9 and page 72, line 25, through 73, line 5, which discloses that a therapeutically effective amount includes an amount sufficient to reduce a clinically significant deficit in the recited activity function, or response of the host by at least about 15 percent, at least 50 percent, by at least 90 percent, or to prevent such a deficit. A therapeutically effective amount is disclosed to alternatively comprise an amount sufficient to cause an improvement in a clinically significant condition in the host by, for example, these benchmark values. The instant application also discloses that treatment of, for example, abnormal elevation of body weight is a clinically significant condition for which a therapeutically effective amount of the recited OB-encoding vectors may be administered in the claimed methods in order to achieve a decrease in body weight (see, e.g., page 11, lines 5-8). Therefore the recitation of a "therapeutically effective amount" enjoys satisfactory written description support in the application as filed (see, e.g., Applicant's response filed October 31, 2007, page 30, lines 10 – 30). Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.


CONCLUSION

All bases for the Examiner's rejections found in the instant Office Action have been address by the foregoing remarks. Applicant respectfully requests that the rejections be withdrawn and the claims allowed.

If any additional fee associated with this communication is due, the Commissioner is hereby authorized to charge payment to Applicant's Deposit Account No. 19-4293. Additionally, the Commissioner is hereby authorized to charge payment or credit overpayment of any fees during the pendency of this application to Applicant's Deposit Account No. 19-4293.

Respectfully submitted,

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